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ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/712,365	EVERY ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/24/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-31 are pending.

Specification

The abstract of the disclosure is objected to because it exceeds the maximum word limit of 150 words. Correction is required. See MPEP § 608.01(b).

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The use of the trademark TEFLON® (on pages 24-27) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Venkataraman (US 2001/0039262 A1) in view of Bartus et al. (U.S. Patent No. 6,514,482) in further view of Byron (US 2004/0016427).

Applicant's independent claim 1 is drawn to a method of treating edema comprising the step of administering a therapeutically effective amount of an orally inhalable diuretic condensation aerosol to a person with edema. Claim 2 limits the treatment to edema associated, at least in part, with a cause selected from a group including congestive heart failure. Claim 3 limits the orally inhalable diuretic to compounds from the group consisting of bumetanide, ethacrynic acid, muzolimine, spironolactone, triamterene, tripamide, BG 9928, and BG 9719. Claim 4 further limits the diuretic of claim 3 to bumetanide. Claim 5 limits the diuretic condensation aerosol of claim 1 to a MMAD in the range of about 1-3 microns. Claim 6 further limits the method of claim 1, by requiring that the diuretic achieve a C_{max} in 10 minutes or less

after administration of the aerosol. Claim 7 limits the administration of the diuretic condensation aerosol in the method of claim 1 to a single inhalation. Claim 8 limits the administration of the diuretic condensation aerosol in the method of claim 1 to more than one inhalation. Independent claim 9 is drawn to a method of making a condensation aerosol comprising the steps of (1) providing a diuretic composition and (2) vaporizing the diuretic composition by heating to form a vapor. Claim 10 limits the diuretic composition to a diuretic selected from the group consisting of bumetanide, ethacrynic acid, muzolimine, spironolactone, triamterene, tripamide, BG 9928, and BG 9719. Claim 11 limits the diuretic to bumetanide and claim 12 limits the method of claim 9 to a diuretic composition further comprising a pharmaceutically acceptable excipient. Claims 13-16 are drawn to diuretic condensation aerosols comprising a diuretic selected from the group consisting of bumetanide, ethacrynic acid, muzolimine, spironolactone, triamterene, tripamide, BG 9928, and BG 9719 (claim 13), wherein the diuretic condensation aerosol is bumetanide (claim 14); wherein the aerosol comprises at least 50% by weight of diuretic condensation particles (claim 15); wherein the diuretic condensation aerosol is substantially free of thermal degradation products (claim 16). Claims 17-20 are drawn to kits comprising a diuretic compound in unit dose form and a device for forming a diuretic aerosol (claim 17); wherein the composition further comprises a pharmaceutically acceptable excipient (claim 18); wherein the diuretic is selected from the group consisting of bumetanide, ethacrynic acid, muzolimine, spironolactone, triamterene, tripamide, BG 9928, and BG 9719 (claim 19); and wherein the diuretic is bumetanide (claim 20). Claims 21-24 are drawn to methods of treating edema by orally administering an inhalable diuretic aerosol; wherein the diuretic aerosol has a MMAD range of about 1-3 microns; wherein a peak plasma level of at least 30 ng/mL is achieved in less

than 10 minutes; wherein the diuretic compound is a loop diuretic (claim 22); wherein the loop diuretic is bumetanide (claim 23), and wherein the edema is associated at least in part with congestive heart failure (claim 24). Claim 25 is drawn to the method of claim 21 further comprising the steps of (1) obtaining a weight measurement of the person with edema prior to administering a diuretic aerosol and (2) using the weight measurement to assess whether to administer a diuretic aerosol. Claims 26-31 are drawn to methods of treating congestive heart failure by orally administering an inhalable loop diuretic condensation aerosol to a person with congestive heart failure exacerbation (claim 26); wherein the loop diuretic is selected from the group consisting of bumetanide, ethacrynic acid, torsemide, and furosemide (claim 27); wherein the loop diuretic condensation aerosol has a MMAD range of about 1-3 microns (claim 28); wherein the loop diuretic achieves a Cmax in ≤ 10minutes (claim 29); wherein the administration of a loop diuretic is affected in a single inhalation (claim 30); wherein the administration of a loop diuretic is affected in more than one inhalation (claim 31).

Venkataraman teaches congestive heart failure is characterized by venous stasis and reduced outflow of blood from the heart. There are typical hemodynamic, renal, and neurohumoral responses, characterized by symptoms, including **edema in the lower portions of the body** (paragraph 008).

Venkataraman teaches **treatment with diuretics** provides effective symptomatic relief of moderate to severe **congestive symptoms of heart failure** (HF) resulting from venous stasis and reduced outflow of blood. The agents improve symptoms and functional capacity by promoting excretion of sodium and water, and helping to lower the plasma volume, which reduces

congestion in the pulmonary and systemic vascular systems. **Diuretics** may improve ventricular function even in asymptomatic patients (paragraph 0009).

Venkataraman teaches **loop diuretics** are considered safer and may provide better patient response than thiazide diuretics and are often more effective in patients with advanced symptoms of **congestive heart failure** (CHF). The most commonly used loop diuretics are **ethacrynic acid,** furosemide **and bumetanide** (paragraph 0010).

Venkataraman teaches potassium sparing diuretics are ordinarily used in combination with thiazides or **loop diuretics** to restrict potassium losses and sometimes augment diuretic action. **Spironolactone** is an example of a potassium sparing diuretic (paragraph 0011).

Venkataraman teaches that his invention comprises injectable and noninvasive routes for agent delivery, including but not limited to, **oral, nasal, pulmonary**, etc. routes (paragraph 0020).

Venkataraman teaches that the route of administration for agents is **chosen according to the speed of absorption desired** and the site of action of the agent (paragraph 0061).

Venkataraman teaches that the methods of administration of the present invention can vary within limits. The frequency of administration of treatment depends upon the patient condition, mode of delivery and concentration of active agent. **Cardiac treatment can be delivered as often as needed** (ql), four times daily (qid), daily (qd) or at certain times in a 24 hour cycle such as after eating or at bedtime (paragraph 0067).

Venkataraman teaches compositions comprising **combinations of at least two or more agents** comprising ACE inhibitors, **loop diuretics and potassium sparing diuretics** in a single administrative dose for **treatment of cardiac indications**. The formulations include those

suitable for **oral and nasal administration** and may be presented in **unit dosage form,** prepared by conventional pharmaceutical techniques, including the step of bringing into association the active ingredient and the pharmaceutical carrier(s) or **excipient(s)** (paragraph 0100).

Venkataraman implicitly suggests the pulmonary administration by inhalation of diuretics, but lacks an explicit teaching of administration by inhalation. Venkataraman also lacks the teaching of an aerodynamic diameter range and a C_{max} in 10 minutes or less after administration of the aerosol, the administration of condensation aerosols, and particle size.

Bartus teaches a method for the **pulmonary delivery** of a medicament to a patient's respiratory tract (abstract and column 3, lines 24-27).

Bartus teaches particles having an **aerodynamic diameter between about 1 micron and about 5 microns** (column 3, lines49-50). This range encompasses the stated MMAD in claim 5.

Bartus teaches the administration to the respiratory tract is preferably by a dry powder **inhaler** or by a metered dose inhaler (column 3, lines 61-62). Both of these administration routes require inhalation.

Bartus teaches combination of drugs and combination of excipients can be prepared and administered (column 7, lines 22-23).

Bartus teaches one embodiment of his invention involves delivery to the pulmonary system of particles in a **single, breath-actuated step** (i.e. a single inhalation) (column 8, lines 20-22).

Bartus teaches a preferred embodiment of his invention is that the **optimal therapeutic concentration is achieved in less than 10 minutes** (i.e. $C_{max} < 10$ minutes) (column 8, lines 47-48).

Byron teaches the formation of aerosols by supplying a material in liquid form to a flow passage and **heating the flow passage such that the material volatizes** and expands out of an open end of the flow passage. The volatized material combines with ambient air such that volatized material **condenses to form the aerosol.** An apparatus and method for generating such an aerosol are disclosed (abstract).

Byron teaches it is often desirable to treat respiratory ailments with, or deliver medicaments by means of, aerosol sprays of finely divided particles of liquid and/or solid, such as powders, liquid medicaments, and the like, which are inhaled into a patient's lungs (paragraph 0002).

Byron teaches that the aerosol generator of his invented apparatus produces small particles (**submicron sized**) and that the use of a space chamber with the aerosol generator can **increase the average particle size of ≤ 0.50 mm to greater than 0.50 mm, preferably to at least about 1.0 μm or greater, and more preferably to about 1.0-5.0 μm** (paragraphs 0056-0057).

Byron teaches that the optimum spacer chamber size and shape can be selected based on the material to be delivered and the desired particle size (paragraph 0059).

Byron teaches that the characteristics of the aerosol generated by the aerosol generator according his invention are generally functions of various parameters of the aerosol generator and the liquid material supplied to the aerosol generator. For aerosols intended for inhalation, for example, it is desirable for the aerosol to be at approximately body temperature when inhaled and for the mass median aerosol diameter of particles of the aerosol to be less than 2 microns,

preferably between 0.2 and 2 microns, and more preferably between 0.2 and 1 micron (paragraph 0074).

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Venkataraman and Bartus to obtain pharmaceutically acceptable diuretic condensation aerosols, because the pulmonary route of administration of a therapeutic agent suggested by Venkataraman implies the inhalation of said agent through either the nose or the mouth; and Bartus teaches the pulmonary administration of medicaments via inhalation. A person of ordinary skill would have been motivated to use Byron's method of making condensation aerosols of the compositions resulting from the combination of the teachings of Venkataraman and Bartus, because Byron teaches how to make condensation aerosols by heating and vaporizing a liquid drug formulation to obtain aerosol particles having average sizes of less than 5 microns. Byron also teaches that his invented apparatus can be modified to obtain particles with optimized average sizes, preferably between 0.2 and 1 micron. A skilled artisan would have appreciated that aerosols are a preferred composition form for the administration of drugs via inhalation, as taught by Byron. A skilled artisan would have been motivated to use condensation aerosols containing at least 50% by weight of the active agent and which were substantially free of thermal degradation products to optimize the dosage effectiveness.

A person of ordinary skill in the art would have been aware that loop diuretics are used to treat edema associated at least in part with congestive heart failure; loop diuretics are generally safer than other alternatives (e.g. thiazides), and that commonly administered loop diuretics include bumetanide and ethacrynic acid, all of which would motivate one to administer

bumetanide to a patient with edema. Skilled artisans at the time of the instant invention would have known that the number of inhalations required for the patient to receive a therapeutically effective amount of a drug would vary according to the patient's medical needs, condition, symptoms and drug concentration. Therefore, it is recognized in the art that a therapeutically effective amount of a drug could be delivered with a single inhalation (taught by Bartus) or after more than one inhalation. A person of ordinary skill in the art would have known that one could administer Venkataraman's compositions to treat congestive heart failure (CHF), especially edema associated in part with CHF. The artisan would have been motivated to use loop diuretics, because loop diuretics are generally safer than other alternatives (e.g. thiazides) and have been used in the treatment of CHF-associated edema per Venkataraman's teachings. Skilled artisans would appreciate that edema is associated with the retention of excess fluid in the body and would know that one could use a patient's weight measurements to assess whether to administer a therapeutically effective amount of a diuretic or diuretics. One would also have known from Venkataraman's teachings that bumetanide is one of the most commonly used loop diuretics. It would have been apparent to the skilled artisan that administration of an inhalable diuretic condensation aerosol would lead to a rapid increase in drug plasma levels (i.e. Cmax < 10 minutes, as taught by Bartus) to levels of at least 30 ng/mL and that the diuretic could be administered in a single inhalation (Bartus) or more than one inhalation as needed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 9 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 12 of copending Application No. 10/057,197 (PG-PUB 2003/0062042). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping in the scope of the steps of the claimed method.

Independent claim 9 of the instant application is drawn to a method of forming a diuretic condensation aerosol comprising the steps of (1) providing a diuretic composition; and (2) vaporizing the diuretic composition, wherein the step of vaporizing comprises the step of heating the composition to form a vapor.

Independent claim 12 of copending '197 is drawn to a method of generating an aerosol comprising the steps of (1) moving a physiologically active compound into a heating-vaporization zone and heating the compound to vaporize at least a portion of said compound; and (2) mixing the vapor with a gas in a ratio, wherein the ratio of vapor to gas is controlled by regulating the rate of vaporization, and wherein the vaporization rate is controlled by changing the rate said compound is moved into the zone, to form a desired particle size when a stable concentration of particles in the gas is reached.

It would have been obvious to a person of ordinary skill at the time of the instant invention that claim 9 of the instant invention is overlapping in scope with claim 12 of copending '197, because both claims involve the steps of heating a composition to form a vapor with the goal of generating an aerosol. A skilled artisan would have been motivated to incorporate the steps of claim 12 of copending '197 to make a diuretic condensation aerosol, because the essential steps of providing a composition and vaporizing said composition by heating are the same as those of claim 9 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 9 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 28 of copending Application No. 10/146,086 (PG-PUB 2003/0209240). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping in scope.

Independent claim 9 of the instant application has been described above.

Independent claim 28 of copending '086 is drawn to a method for aerosolizing a drug (i.e. making a drug aerosol) comprising the steps of (1) providing a rigid substrate having an interior surface surrounding an interior region and an exterior surface; (2) coating a vehicle containing at least one drug onto the exterior surface of the rigid substrate; (3) locating a combustible filament in the interior region of the rigid substrate; and (4) igniting the combustible filament in the interior region to heat the exterior surface of the rigid substrate and vaporize the drug coated thereon.

It would have been obvious to a person of ordinary skill at the time of the instant invention that claim 9 of the instant invention is overlapping in scope with claim 28 of copending '086, because both claims involve the steps of heating a composition to form a vapor to generate an aerosol. A skilled artisan would have been motivated to incorporate the steps of claim 28 of copending '086 to make a diuretic condensation aerosol, because the essential steps of providing a drug composition and vaporizing said composition by heating are the same as those of claim 9 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 9-11 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12 and 18 of copending Application No. 10/633,876. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping in scope.

Claims 9-11 of the instant application have been described *supra*. Claim 10 further limits claim 9 by specifying that the diuretic composition comprises a diuretic selected from the group consisting of bumetanide, ethacrynic acid, furosemide, muzolimine, spironolactone, torsemide, triamterene, tripamide, BG 9928, and BG 9719. Claim 11 further limits the diuretic of claim 10 to bumetanide.

Independent claim 12 of copending '876 is drawn to a method for producing a condensation aerosol comprising (1) heating a substrate having a drug composition film on the surface to a temperature > 300 °C; (2) substantially volatilizing the drug composition film from

the substrate in a period of 2 seconds or less; and (3) flowing air across the volatilized drug composition, under conditions to produce an aerosol containing less than 10 % by weight drug composition degradation products and at least 50% of the drug composition in said film. Claim 18 of copending '876 limits the drug composition film to a group of drugs, including a **bumetanide film** with a thickness between 0.1 and 5 microns (item 4 of said group).

It would have been obvious to a person of ordinary skill at the time of the instant invention that claims 9-11 of the instant invention are overlapping in scope with claims 12 and 18 of copending '876, because these claims involve the steps of heating a composition to form a vapor and generate an aerosol. A skilled artisan would have been motivated to incorporate the steps of claim 12 and 18 of copending '086 to make a diuretic condensation aerosol, because the essential steps of providing a drug composition (i.e. a bumetanide film) and vaporizing said composition by heating are the same as those of claim 9 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 9-11 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 15 and 21 of copending Application No. 10/633,877. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping in scope.

Claims 9-11 of the instant application have been described *supra*.

Independent claim 15 of copending '877 is drawn to a method for producing a condensation aerosol comprising (1) heating a substrate in the article of claim 1 having a drug composition film on the surface to a temperature between 300-500 °C; (2) vaporizing the drug composition film from the substrate in a period of 2 seconds or less; and (3) flowing a gas across the volatilized drug composition at a gas flow rate effective to produce a desired size of aerosol particles by condensation, containing less than 10 % by weight drug composition degradation products and at least 50% of the drug composition in said film. Claim 21 of copending '877 limits the drug composition film to a group of drugs, including a **bumetanide film** with a thickness between 0.1 and 5 microns (item 4 of said group).

It would have been obvious to a person of ordinary skill at the time of the instant invention that claims 9-11 of the instant invention are overlapping in scope with claims 15 and 21 of copending '877, because these claims involve the steps of heating a composition to form a vapor and generate an aerosol. A skilled artisan would have been motivated to incorporate the steps of claim 15 and 21 of copending '087 to make a diuretic condensation aerosol, because the essential steps of providing a drug composition (i.e. a bumetanide film) and vaporizing said composition by heating are the same as those of claim 9 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 11, 13, 14, and 17-20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 74,

79, and 82 of copending Application No. 10/718,982 in view of Venkataraman (US 2001/0039262 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping in scope.

Claim 11 of the instant application has been described *supra.*

Independent claim 13 is drawn to a diuretic condensation aerosol comprising a diuretic selected from the group consisting of bumetanide, ethacrynic acid, furosemide, muzolimine, spironolactone, torsemide, triamterene, tripamide, BG 9928, and BG 9719 and wherein the diuretic condensation aerosol has a MMAD in the range of 1-3 microns. Claim 14 limits the diuretic of claim 13 to bumetanide. Independent claim 17 is drawn to a kit for delivering a diuretic condensation aerosol comprising a composition comprising a diuretic compound in a unit dose form; and a device for forming a diuretic aerosol, wherein said device comprises an element configured to heat the composition to form a vapor, an element allowing the vapor to condense – forming a condensation aerosol- and an element permitting a user to inhale the condensation aerosol. Claim 18 further limits the composition contained within the kit of claim 17 to further comprise a pharmaceutically acceptable excipient. Claim 19 limits the diuretic compound contained within the kit of claim 17 to one selected from the group consisting of bumetanide, ethacrynic acid, furosemide, muzolimine, spironolactone, torsemide, triamterene, tripamide, BG 9928, and BG 9719. Claim 20 limits the diuretic compound of claim 19 to bumetanide.

Independent claim 1 of copending '982 is drawn to a composition for delivery of a drug wherein the condensation aerosol is formed by heating a drug composition to form a vapor, and condensing the vapor to form a condensation aerosol comprising the drug, wherein the

condensation aerosol comprises particles that are characterized by less than 10 % by weight, wherein the condensation aerosol has an MMAD of less than 5 microns, and wherein the drug is heat stable. Claim 2 '982 limits the heat stable drug composition to a group of drugs, including **bumetanide, spironolactone, and triamterene**. Claim 4 limits the composition of claim 1 to one wherein less than 5% degradation products characterize the condensation aerosol particles and the heat stable drug is selected from a group including **bumetanide, spironolactone, and triamterene.**

Independent claim 74 is drawn to a kit comprising (a) a thin film of a drug composition comprising a drug, on a solid support, and (b) a device for providing the condensation aerosol, which is formed by heating the drug composition to produce a vapor, and condensing the vapor to form a condensation aerosol comprising a heat stable drug, wherein the condensation aerosol comprises particles characterized by less than 10 % drug degradation products by weight and having a MMAD of less than 5 microns. Claim 75 further limits the drug composition film of claim 74 to one with a thickness between 0.5 and 20 microns. Claim 76 further limits the kit of claim 74 to one wherein the device comprises a heating element configured to heat the thin film to produce a vapor, and an enclosure allowing the vapor to condense to form a condensation aerosol. Claim 82 limits the heat stable drug of claim 74 to one selected from the group including, **bumetanide, ethacrynic acid, spironolactone, and triamterene**.

Venkataraman teaches that loop diuretics are considered safer than thiazide diuretics and the most commonly used loop diuretics include **bumetanide** (paragraph 0010).

It would have been obvious to a person of ordinary skill at the time of the instant invention that claims 11, 13, and 14 of the instant invention are overlapping in scope with claims

1, 2, and 4 of copending '982, because these claims are drawn to compositions comprising bumetanide as the heat stable diuretic drug. A skilled artisan would have appreciated that the kits of claims 17-19 of the instant application have the same limitations as the kits of claims 74, 79, and 82 of copending '982. Regarding claim 20 of the instant application in which the diuretic is bumetanide, it would have been obvious to a person of ordinary skill in the art that one could use bumetanide in the kit of claim 82 copending '982, because bumetanide is a member of the group of heat stable drugs listed in said claim. A skilled artisan would have been motivated to use bumetanide in a kit, because it is a commonly used loop diuretic and loop diuretics are safer than thiazide diuretics.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 13 and 19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 19 of copending Application No. 10/768,205. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are either anticipated or obvious over the claims of the copending application, '205. Claim 13 of the instant application is obvious over claim 1 of copending application 10/768,205 (drawn to condensation aerosols comprising a drug ester), because spironolactone, which is part of the group of drugs listed in claim 13 of the instant application, is a lactone. Lactones are cyclic esters (See Solomons, T. W. G. *Organic Chemistry, 5th ed.* John Wiley & Sons, Inc.: New York, 1992, p 784).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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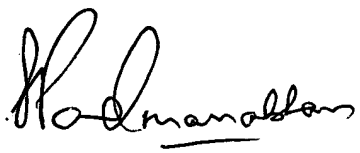

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